BÖLÜM 29

Kolorektal Kanser ve Epigenetik

Zuhal ALTINTAŞ[1]

Giriş

Kanser, hücresel çoğalma, hücre metabolizması, anjiyogenez, hücre ölümü, invazyon, metastaz gibi temel süreçleri düzenleyen mekanizmaların bozulması sonucu gelişir (1). Kanser sadece genetik bir hastalık değildir. Kanserin progesyonunda bağışıklık sistemi, tümör mikroçevresi ve epigenetik gibi kişinin ek biyolojik süreçler de etkilidir (2). Kanser genetik ve/veya epigenetik değişikliklerin birikimi ile oluşan, çok adımlı kompleks bir hastalıktır.

Uluslararası Kanser Araştırmaları Ajansı (IARC) GLOBOCAN 2020 yılı kanser istatistiklerine göre kanser, bütün dünyada sağlık problemleri içinde önemli bir yer teşkil etmektedir ve gelişmiş ülkelerdeki istatistiklere göre kalp hastalıklarından sonra en çok ölüme yol açan ikinci hastalık olarak değerlendirilmektedir (3).

Kolorektal kanser (KRK), karaciğer kanseri, mide kanseri, pankreas kanseri ve özofagus kanseri, dünya çapında kansere bağlı ölümlerin önde gelen nedenleridir. Gastrointestinal maligniteler, bazı kanserlerden daha düşük insidansa sahip olmasına rağmen dünyada ikinci sırada ölüme neden olan kanserlerdir (4).

DNA metilasyonu, mutasyon veya delesyon gibi genetik değişikliklere işlevsel olarak eşdeğer olan genomda ılımlı ve potansiyel olarak geri döndürülebilir bir değişiklik olarak kabul edilir (5). Epigenetik, primer DNA dizisini değiştirmeden, mitotik ve/veya mayotik olarak kalıtılabilen gen fonksiyon değişiklikleri olarak bir başka deyişle DNA dizisinde değişiklik içermeyen kalıtsal fenotipik değişiklikleri ifade eder (6).

Epigenetik, genomik fonksiyon ve aktiviteye rehberlik eden genom üzerine kodlanmış ikinci bir bilgi katmanıdır. Epigenetik iki mekanizma ile hareket eder:

1. Genomun ve/veya protein-DNA etkileşimlerinin 3 boyutlu yapısını değiştiren kromozomal proteinlerdeki modifikasyonlar ve
2. DNA zincirinin kendisinin kimyasal modifikasyonu (7).

[1] Dr. Öğr. Üyesi, Mersin Üniversitesi Tıp Fakültesi Tıbbi Genetik AD, e-mail: altintaszmertgmail.com

değiştiricilerin faydasını kanıtlamıştır. Epigenetik değişiklikler değiştirilmiş ifadeler, KRK'de tedavi yanıtının teşhisi, prognozu ve tahmini için biyobelirteçler olarak kullanılabilir. DNA metilasyonuna dayalı biyobelirteçler ticarileştirilmiş ve bu biyobelirteçlerin bazıları klinik uygulamaya ve KRK'deki kılavuzlara şimdiden girmiştir. Son olarak, artan bu potansiyel belirteçler hakkında çok az şey bildirildiğinden, dolaşımdaki DNA metilasyonunun öngörücü rolünü bulmak için daha fazla araştırmaya ihtiyaç vardır

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